

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12N 5/10, 15/62, 15/85, A61K 48/00, A61P 35/00 // C07K 16/28, 14/705, 16/00	A3	(11) International Publication Number: WO 00/23573 (43) International Publication Date: 27 April 2000 (27.04.00)
(21) International Application Number: PCT/US99/24484 (22) International Filing Date: 20 October 1999 (20.10.99) (30) Priority Data: 60/105,014 20 October 1998 (20.10.98) US (71) Applicant: CITY OF HOPE [US/US]; 1500 East Duarte Road, Duarte, CA 91010-0269 (US). (72) Inventors: RAUBITSCHKEK, Andrew; 1691 El Molino, San Marino, CA 91108 (US). JENSEN, Michael, C.; 2305 Woodlyn Road, Pasadena, CA 91104 (US). WU, Anna, M.; 14919 Sutton Street, Sherman Oaks, CA 91403 (US). (74) Agents: KERR, Don, M. et al.; Rothwell, Figg, Ernst & Kurz, Suite 701 East, 555 13th Street N.W., Columbia Square, Washington, DC 20004 (US).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 8 September 2000 (08.09.00)
(54) Title: CD20-SPECIFIC REDIRECTED T CELLS AND THEIR USE IN CELLULAR IMMUNOTHERAPY OF CD20 ⁺ MALIG- NANCIES (57) Abstract <p>Genetically engineered, CD20-specific redirected T cells expressing a cell surface protein having an extracellular domain comprising a receptor which is specific for CD20, an intracellular signaling domain, and a transmembrane domain. Use of such cells for cellular immunotherapy of CD20⁺ malignancies and for abrogating any untoward B cell function. In one embodiment, the cell surface protein is a single chain FvFc:ζ receptor where Fv designates the V_H and V_L chains of a single chain monoclonal antibody to CD20 linked by peptide, Fc represents a hinge-CH₂-CH₃ region of a human IgG₁, and ζ represents the intracellular signaling domain of the zeta chain of human CD3. A method of making a redirected T cell expressing a chimeric T cell receptor by electroporation using naked DNA encoding the receptor.</p>		

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/24484

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N5/10 C12N15/62 C12N15/85 A61K48/00 A61P35/00
//C07K16/28,C07K14/705,C07K16/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	M. JENSEN ET AL.: "CD20 is a molecular target for scFvFc:zeta receptor redirected T cells: implications for cellular immunotherapy of CD20+ malignancy." BIOLOGY OF BLOOD AND MARROW TRANSPLANTATION, vol. 4, no. 2, 1998, pages 75-83, XP000910525 Charlottesville, VA, USA the whole document --- -/--	1-34

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

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- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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Date of the actual completion of the international search

17 May 2000

Date of mailing of the international search report

30/05/2000

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/24484

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	H. ABKEN ET AL.: "Can combined T-cell- and antibody-based immunotherapy outsmart tumor cells?" IMMUNOLOGY TODAY, vol. 19, no. 1, January 1998 (1998-01), pages 1-5, XP004101455 Amsterdam, The Netherlands the whole document	1-34
Y	H. HAISMA ET AL.: "Construction and characterization of a fusion protein of single-chain anti-CD20 antibody and human beta-glucuronidase for antibody-directed enzyme prodrug therapy." BLOOD, vol. 92, no. 1, 1 July 1998 (1998-07-01), pages 184-190, XP002076505 New York, NY, USA abstract	1-34
Y	WO 97 23613 A (CELLTECH THERAPEUTICS LTD.) 3 July 1997 (1997-07-03) figures 1,2A,14,15 claims page 18, line 14 - line 29 page 19, line 26 -page 20, line 5	1-34
Y	WO 94 11026 A (IDEC PHARMACEUTICALS CORPORATION) 26 May 1994 (1994-05-26) examples claims	1-34
Y	WO 98 41613 A (G. OTTEN ET AL.) 24 September 1998 (1998-09-24) examples claims	1-34
A	D. ANDERSON ET AL.: "Targeted anti-cancer therapy using rituximab, a chimaeric anti-CD20 antibody (IDEC-C2B8) in the treatment of non-Hodgkin's B-cell lymphoma." BIOCHEMICAL SOCIETY TRANSACTIONS, vol. 25, 1997, pages 705-708, XP002078838 the whole document	1-34

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INTERNATIONAL SEARCH REPORT

Int. l. Application No

PCT/US 99/24484

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>G. GROSS ET AL.: "Endowing T cells with antibody specificity using chimeric T cell receptors." THE FASEB JOURNAL, vol. 6, no. 15, December 1992 (1992-12), pages 3370-3378, XP002137900 Bethesda, MD, USA cited in the application page 3376, left-hand column, line 17 - line 51 figure 1</p>	1-34
A	<p>US 5 359 046 A (CAPON ET AL.) 25 October 1994 (1994-10-25) example 3 claims</p>	1-34
P,X	<p>M. JENSEN ET AL.: "Specific recognition and lysis of CD20+ lymphoma cells by primary human CD8+ CTL clones genetically modified to express a CD20-specific chimeric immunoreceptor." BLOOD, vol. 92, no. 10, suppl. 1 (part 1 of 2), 15 November 1998 (1998-11-15), page 245a XP000906991 New York, NY, USA abstract # 998</p>	1-34

INTERNATIONAL SEARCH REPORT

international application No.

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 17-20 and 30-34 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/24484

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9723613 A	03-07-1997	AU 1201997 A CA 2238873 A EP 0870019 A JP 2000502562 T	17-07-1997 03-07-1997 14-10-1998 07-03-2000
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